A Dissertation on

LIVER BIOCHEMICAL PROFILES IN CONGESTIVE HEART FAILURE

Dissertation Submitted to

THE TAMILNADU Dr.M.G.R. MEDICAL UNIVERSITY
CHENNAI - 600 032

with partial fulfillment of the regulations
for the award of the degree of

M.D. GENERAL MEDICINE
BRANCH-I

INSTITUTE OF INTERNAL MEDICINE,
MADRAS MEDICAL COLLEGE
CHENNAI - 600 003.

MARCH 2007

CERTIFICATE

This is to certify that this dissertation in **"LIVER BIOCHEMICAL PROFILES IN CONGESTIVE HEART FAILURE"** was a work done by **Dr.C.SANKAR**, under my guidance during the academic year 2004-2007. This has been submitted in partial fulfillment of the award of M.D.Degree in General Medicine (Branch-I) by the Tamil Nadu Dr.M.G.R. Medical University, Chennai- 600 032.

Prof.P.Thirumalai Kolundu Subramanian, M.D.,
Director, Prof. & Head.,
Institute of Internal Medicine,
Madras Medical College &
Govt. General Hospital
Chennai - 600 003.

The DEAN
Madras Medical College &
Govt. General Hospital
Chennai-600 003.

DECLARATION

I solemnly declare that this dissertation entitled **"LIVER BIOCHEMICAL PROFILES IN CONGESTIVE HEART FAILURE"** was done by me at Madras Medical College and Government General Hospital during the academic year 2004-2007 under the guidance and supervision of **Prof.P.Thirumalai Kolundu Subramanian, M.D.,** This dissertation is submitted to the Tamil Nadu Dr.M.G.R. Medical University, towards the partial fulfillment of requirement for the award of M.D.Degree in General Medicine (Branch-I)

Place :

Date : **Dr.C.SANKAR**

ACKNOWLEDGEMENT

I am immensely grateful to my client, **Prof.P.Thirumalai Kolundu Subramanian, M.D**., Director, Professor and Head, Institute of Internal Medicine, for his inspiring comments and guidance in making this study possible.

I express my sincere gratitude to my former Directors, **Prof.S.Tamilvanan, M.D.,** and **Prof. D.Dhanaseelan Jayakumar, M.D.,** for their guidance and encouragement.

I sincerely thank **Prof.A.Manamalli, M.D.,** Director, Professor and Head, Institute of Biochemistry for granting me permission for carrying out the investigations required for the study.

I wish to express my thanks to my Assistant Professors, **Dr.K.V.S.Latha, M.D., Dr.R.Penchalaiah, M.D.,** and **Dr.P.Vijayaragavan, M.D.,** for their valuable suggestions and support.

I am thankful to all participants of study and control group for their co-operation.

SPECIAL ACKNOWLEDGEMENT

I grateful acknowledge and sincerely thank **Prof.Kalavathi Ponniraivan, B.Sc., M.D.,** Dean, Madras Medical College and Government General Hospital, Chennai, for granting me permission to utilize the resources of the institution for my study.

CONTENTS

Sl. No.	Title	Page No.
1.	INTRODUCTION	1
2.	AIMS OF THE STUDY	2
3.	REVIEW OF LITERATURE	3
4.	MATERIALS AND METHODS	21
5.	RESULTS	34
6.	DISCUSSION	44
7.	SUMMARY	55
8.	CONCLUSION	57
9.	BIBLIOGRAPHY	
10.	ABBREVIATIONS	
11.	PROFORMA	
12.	MASTER CHART	

INTRODUCTION

Liver, the largest gland in the body has many complex functions. For the liver to perform its primary functions, high rates of blood flow and close contact between sinusoids and hepatocytes are essentials.

As a result of its complex vascular supply and high level of metabolic activity, the liver is uniquely vulnerable to a broad spectrum of circulatory disturbances.

Heart failure, causes a number of pathophysiological effects which, alone or in combination result in liver cell damage. As a consequence, liver function abnormalities are so common in heart failure.

Liver dysfunction in heart failure is usually mild and asymptomatic and often detected incidentally on routine liver biochemical investigations.

Present study was undertaken, mainly to emphasize the importance of early identification of liver serum biochemical markers in heart failure patients. Liver biochemical tests are found to be very useful in assessing the duration and severity of heart failure. Early and adequate treatment of the underlying cause of heart failure reverts liver function derangements to normal and prevents permanent liver damage.

AIMS OF THE STUDY

1. To study the influence of congestive heart failure on liver biochemical profiles.

2. To assess the changes in liver biochemical tests in relation to the duration of heart failure.

LITERATURE REVIEW

ANATOMY AND PHYSIOLOGY

Liver is richly supplied with blood and received fully 25% of the total cardiac output. Two thirds of the blood flow to the liver is supplied by the portal vein which is relatively lacking in oxygen. By contrast, the hepatic artery, which supplies only about one third of the total hepatic blood flow, carries oxygen–rich blood and accounts for more than 50% of the oxygen delivered to the liver; it also provides the sole blood supply to the major bile ducts[(1)] .

The functional unit of the liver is the hepatic acinus, which consists of a cluster of hepatocytes, grouped around hepatic arterioles and portal venules[(1)] . The centre of the acinus (periportal region) is known as zone 1, the periphery (perivenular region) as zone 3, the region in between as zone 2[(2)].

Zone 1 receives highest levels of oxygen whereas zone 3 receives relatively hypoxic blood. The gradient is exaggerated in the setting of vascular collapse, when extraction of oxygen by zone 1 cells is increased to compensate for the reduction in hepatic blood flow and results in lower than normal oxygen tension in zone 3[(3)]. Unlike portal venous flow, which lacks autoregulatory control, hepatic arterial flow is regulated closely to maintain a relatively

constant total hepatic blood flow. So, when portal blood flow diminishes, a rise in the local adenosine concentration results in compensatory arteriolar vasodilation[3] .

LIVER PATHOGENESIS IN CONGESTIVE HEART FAILURE

Three factors are thought to be involved in the pathogenesis of liver function abnormalities:

1. Decreased hepatic blood flow due to decreased cardiac output which can result in hypoxia of the liver [4,5] because of centrilobular damage, especially the zone 3[6].

2. Passive congestion occurs in congestive cardiac failure which results in increased hepatic venous pressure and sinusoidal congestion. The resulting perisinusoidal odema results in decreased hepatic blood flow, atrophy and necrosis of centrilobular cells[3].

Passive congestion alone is insufficient to cause significant hepatic necrosis; decreased hepatic blood flow is also necessary[8]. So cardiac output is the principal determinant of hepatic ischemia[9] . Chronic passive congestion plays a major role in sensitizing the liver to hemodynamic and hypoxic insults.

3. Hypoxic hepatitis (shock liver ; ischaemic hepatitis) refers to diffuse hepatic injury following hypotension or acute hypoperfusion. Most

cases occur in the setting of congestive heart failure, although many other causes are also possible [10,11,12,13].

However, hypoxia per se does not produce centrilobular necrosis. Splanchnic ischaemia may result in absorption of endotoxin from the intestinal lumen, causing portal endotoxaemia which was superimposed on hypoxia to produce centrilobular necrosis [14].

Liver dysfunction in congestive heart failure is usually mild and asymptomatic and often detected incidentally on routine liver biochemical testing. When symptomatic, it may present as mild jaundice. In patients with chronic, severe heart failure, jaundice may be so deep as to suggest biliary obstruction [15]. When jaundice is accompanied by significant AT elevation in patients presenting with acute cardiac decompensation, the clinical picture may simulate that of acute viral hepatitis[16] .

Congestive heart failure results in a broad range of liver biochemical abnormalities. Serum bilirubin is mildly elevated with a high unconjugated fraction[17]. Multiple factors are thought to be contributary including hepatocellular dysfunction, hemolysis, pulmonary infarction, canalicular obstruction secondary to distended hepatic veins, medications and superimposed sepsis[8]. Jaundice of right sided heart failure seems to be clinically and pathophysiologically distinct from that of ischaemic hepatitis[8]. Bilirubin level falls quickly with resolution of failure within three to seven days

[17]. Even in the presence of deep jaundice, the serum alkaline phosphatase level is usually normal or only minimally elevated [18,19], a finding that helps distinguish cardiac from obstructive jaundice. It returns to normal in a week after treatment of failure.

Serum AT levels are mildly elevated usually two to three times normal levels, in up to one third of patients with chronic heart failure [19,20]. In patients with severe, acute heart failure, however, the AT levels may be extremely elevated, simulating those of viral hepatitis[16], especially when the heart failure is complicated by hypotension[8] . However, high serum AT levels have been described in the setting of heart failure with minimal or no hemodynamic instability[9,21]. These probably reflect ischaemic injury secondary to decreased cardiac output because the degree of AT elevation correlates with the extent of zone 3 necrosis on liver biopsy specimens [22]. After the treatment of heart failure, AT levels return to normal within five to ten days[23].

Serum albumin levels are decreased in 30% to 50% of patients with cardiac decompensation. The incidence and degree of change, appear to be similar in acute and chronic failure[19,21] . The serum albumin level does not correlate with the degree of histological damage to the liver [19] . Causes of low albumin probably include decreased hepatic synthesis, leakage from a congested intestine, and poor nutrition. With treatment, albumin level tends to rise over a period of one or more months[24] .

Prolonged prothrombin times are found in 80% to 90% of patients with acute and chronic heart failure [25,17,19] due to decreased hepatic synthesis of vitamin–k dependent clotting factors. It returns to normal in two to three weeks following treatment of the heart failure[24] .

An uncommon complication of sustained chronic congestive cardiac failure is so–called cardiac sclerosis. The pattern of liver fibrosis is mostly centrilobular. The damage rarely fulfills the criteria for the diagnosis of cirrhosis, but the historically sanctified term cardiac cirrhosis cannot easily be dislodged [26].

Cardiac sclerosis was the most common form of hepatic fibrosis, occurring in 48% of cases. Cardiac fibrosis was quite frequent but frank cirrhosis was rarely found[27] .

HISTOLOGICAL ASPECTS

Antony Benivieni (1507) and Gionani Morgagni (1761) through their clinical works “De–Additis nonnilis ac minadis maeborum et Sanationum causis (about many usual and miraculous causes of diseases and their causes) and “De sedibus et causis Morborum per anatomen esidagitis” (about the sites and causes of diseases investigated by anatomy) can be considered to be pioneers in the study of pathology of liver.

"Acute central necrosis" of the liver was first described histologically by Kiernan et al, in 1833 and was initially associated only with severe congestive heart failure. Mallory et al, described the appearance of central congestion with focal necrosis in congestive heart failure.

Garvin et al, in 1943, found 1.7 per cent of 407 patients were thought to have cirrhosis due to heart diseases[28]. In an another study, Koletsky et al, in 1944, found 35 (4.4 per cent) were considered to have cardiac cirrhosis at postmortem among 790 patients dying of heart diseases.

Sherlock et al, 1951, described the clinical and biochemical features of zone 3 necrosis in heart failure. He found lack of correlation between right atrial pressure and the degree of zone 3 necrosis in patients with cardiac decompensation[8]. This is followed by many studies which proved cardiac output is the major determinant of hepatic ischaenia which is the main contributing factor for liver function derangements[9]. Sherlock found jaundice and hepatic synthetic function were no worse in patients with cardiac cirrhosis than in those with simple passive congestion[8].

Bang et al, in 1959, have found serum liver enzymes elevation in congestive heart failure patients. Killip et al, in 1960, described massive elevations of serum AT levels secondary to cardiogenic shock[29] .

Richman et al, in 1961 described liver function test abnormalities in 175 patients with congestive heart failure. They found acute heart failure is associated with more elevation of serum liver enzymes than chronic heart failure. They found even minor impairments of left ventricular function can lead to marked liver enzyme abnormalities[19] . West et al, in 1961, found elevation of AT levels is due to increase in systemic venous pressure, pulmonary capillary wedge pressure, cardiac index and other factors in congestive heart failure. They also found much higher levels of serum alkaline phosphatase are uncommon[18]. In 1962, Logan et al, found very high serum liver enzyme levels, in congestive heart failure. They cautioned misinterpretation of these cases as viral or drug induced hepatitis[16].

Refsum et al, in 1963, found right sided heart failure per se can not cause centrilobular necrosis. They also found no correlation between serum liver enzyme activities and the clinical signs of right heart failure. Yoshiko et al, in 1964, have stressed the importance of enzyme studies besides routine methods which reflect the obstruction and metabolic disturbances of liver cells in causes of congestive heart failure[30].

In contrast to decrease in hepatic blood flow and passive congestion, arterial hypoxia does not appear to be an important cause of liver damage in congestive heart failure, as it is relatively uncommon in this condition[31].

Shorey et al [32] , 1969, and Whelan et al, 1969 found liver biochemical tests were normal in patients with hypoxia due to lung disease without heart failure. Whelan suggested that a degree of heart failure is necessary to produce abnormalities of liver function test. Heart failure may play a part in causing centrilobular liver all necrosis[33]. Xarau et al, 1979, found the co existence of both factors was necessary. Dunn et al, 1973 described congestive hepatopathy and liver function abnormalities. In their study they have found 95% of patients had hepatomegaly, 20% had jaundice, 70% had elevated serum bilirubin levels and 12 to 33% had elevated serum AT levels[17].

Bynum et al, in 1979, described elevation of serum liver enzymes more than five times normal in the presence of centrilobular necrosis due to decrease in hepatic blood flow[22]. The above studies, sherlock's and many other studies suggested passive congestion alone is insufficient to cause significant centrilobular necrosis so as to rise serum liver enzymes. There must be significant decrease in cardiac output to produce these changes.

Shock liver (Ischaemic hepatitis) is a severe hepatic derangement following a hypotensive or ischaenic insult[21]. The clinical picture varies from an isolated finding of very high AT levels after an episode of hypotension to fulminant hepatic failure after acute circulatory failure, often in the setting of established chronic heart failure[21]. Jaundice, marked elevation of serum liver enzymes can all occur[29]. It is the duration rather than the cause of the shock

that is important in the development of the syndrome. Shock of less than 24 hours duration rarely causes central liver cell necrosis. Shock of more than 24 hours does so invariably. The term “Ischaemic hepatitis” was introduced by Bynum et al, in 1979, captures the potential clinical resemblance of the entity to viral hepatitis. The histologic hallmark of ischaemic hepathtis is zone 3 necrosis. The presence of chronic heart failure, a recent episode of acute circulatory failure, hepatomegaly, a rapid fall in serum AT levels after the initial rise and additional evidence of end-organ hypoperfusion especially acute tubular necrosis of the kidney with concomitant early rise in serum creatinine level favour a diagnosis of ischaemic hepatitis rather than viral or drug induced hepatitis[21].

Serum albumin is low in about 30 to 50% of patients with congestive heart failure. The incidence and the degree of change appear to be similar in acute and chronic failure. These changes were not marked. In 75% of those with reduced albumin, the values were between 2.5 to 2.9 g/dl [19].

Sherlock in his series of 50 patients with heart failure, found eight patients with marked jaundice, with serum bilirubin levels ranging between 4.5 to 22 mg/dl. Seven of these eight patients had mitral stenosis. He found a correlation of the serum bilirubin level with the right atrial pressure, but not the cardiac output. Therefore, the jaundice of right sided heart failure seems to be clinically and pathophysiologically distinct from that associated with

ischaemic hepatits and results from congestion rather than diminished hepatic perfusion.

Jaundice is found in less than 20% of patients with liver damage due to congestive heart failure, and depends on the severity of the heart failure, as evidenced by right atrial pressure, pulmonary wedge pressure, and cardiac index [(20)]. However serum bilirubin is elevated in 20 to 80% patients with congestive heart failure. The elevated serum bilirubin falls quickly with resolution of heart failure, usually becoming normal within three to seven days. Serum bilirubin level is usually less than 3 mg/dl and it rarely exceeds 5 mg/dl[(19,20)].

Extreme elevation of serum bilirubin and associated AT levels elevation would suggest extensive hepatic hecrosis[(5)].

Gibson et al, in 1984, in their study of liver function tests in patients with likely fall in cardiac output have demonstrated marked rise in serum AT levels and short time course of enzyme elevation lasting 3 – 11 days. They concluded that ischaemic hepatitis was caused by poor hepatic perfusion associated with an acute fall in cardiac output[(12)]. Kisloff et al[(34)], in 1976 and Nouel et al[(21)], 1980, demonstrated fulminant hepatic failure due to transient cirurlatory failure in patients with congestive heart failure.

Kaymakcalan et al, 1978, documented shock liver in congestive heart failure patients. They suggested it is a low cardiac output which causes decreased blood flow and parenchymal hypoxia, which is the main prerequisite for centrilobular necrosis. Shock is an extreme example of a low cardiac output state[35].

In ischaemic hepatitis, Loosli et al, 1981, found rapid elevation of serum AT levels, with peak levels of 8 to 100 times the upper reference limit within 24 hours. They fall rapidly if there is an improvement in the cardiac status, being less than twice normal within about six days. In ischaemic hepatitis serum bilirubin increases in most patients but rarely to more than four times normal. Alkaline phosphatase may increase up to twice normal. The prothombin time is not usually increased by more than two seconds. Serum albumin and proteins are unaffected[12]. Shovman et al, in 1997, documented ischaemic hepatitis resulting from acute hypoxia when low cardiac output further reduces oxygen supply, aggravating underlying congestion due to poor venous outflow. He found elevated AT levels, elevated serum bilirubin level, prolonged prothrombin time and the presence of acute renal failure with reference to ischaemic hepatitis. He included ischaemic hepatitis should be considered whenever acute hepatitis follows a recent episode of systemic hypotension, especially in the context of concomitant congestive heart failure[36].

In 1981, Arcidi et al, studied hepatic morphology in cardiac dysfunction. They have demonstrated chronic passive congestion and centrilobular necrosis potentiate the development of each other[37]. These hepatic manifestations are considered together since both are commonly seen at autopsy because there is an element of preterminal circulatory failure with virtually every death. Right sided cardiac failure leads to passive congestion of the liver. Left sided cardiac failure or shock leads to centribular necrosis. The combination of both produces centrolobular hemorrhagic necrosis known as nutmug liver[26].

In most instances, the only clinical evidence of centrilobular necrosis or its variants is mild to moderate transient elevation of serum AT levels. The parenchymal damage may be sufficient to induce mild to moderate jaundice[26].

Ross et al, in 1981, revealed evidence of centrilobular necrosis and liver function derangements [38].

Nanji et al, found mild to moderate increase in serum AT levels and accompanying hyperbilirubinemia in 1983. They revealed marked increase in serm AT levels may occur rarely and usually preceded by prolonged shock or hypotensive episodes. The enzyme activities get decreased sharply with improvement in patients circulatory status[39].

Kubo et al, in 1987, after his study on liver function abnormalities in chronic heart failure, concluded liver function abnormalities remain common in patients with congestive heart failure but are generally small in magnitude and not associated with clinically apparent hepatic disease. It is likely that reduced forward flow and passive backward congestion, together are the contributing factors in the pathogenesis of these biochemical abnormalities[20].

Mace et al, 1985, in their study of 65 infants and children with hemodynamic abnormalities associated with congenital heart disease noted liver function derangements in most or all of the patients. When patients hemodynamic status improved with treatment, the results of liver function tests returned towards normal[40].

Arora et al, 1993, found a case of acute hepatic failure in constrictive pericarditis[41].

Rober et al, 2002, in their study of cardiac hepatopathy with reference to clinical, hemodynamic, and histologic characteristics, found elevated serum liver AT levels in cardiac dysfunction, particularly in acute cardiac failure. They grouped patients based on duration of cardiac dysfunction [42].

Van Lingen et al, 2005, studied jaundice as a presenting feature of heart failure. They found jaundice due to heart disease tends to be mild. Both

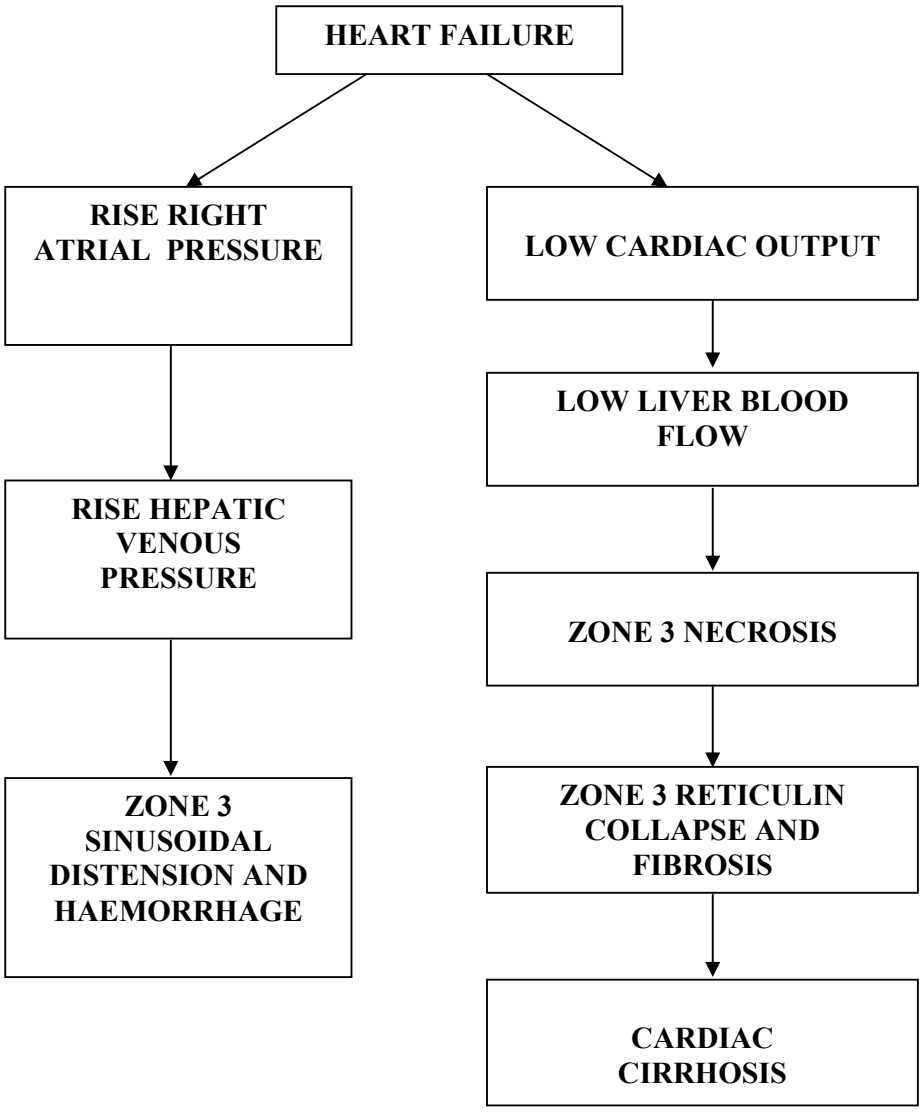
passive congestion and ischaemic hepatits can produce jaundice though due to the former is more common[43].

YEAR	AUTHOR	OBSERVATION
1833	Kiernan et al	Central liver necrosis in congestive heart failure
1911	Mallory et al	Central congestion with focal necrosis in congestive heart failure
1943	Garvin et al	Cirrhosis in heart disease patients
1944	Koletsky et al	Cirrhosis in heart disease patients
1951	Sherlock S. et al	Various anatomical, functional, biochemical changes of liver in heart failure
1959	Bang et al	Elevation of serum liver amiontransferases in heart failure
1969	Killip et al	Elevation of serum liver aminotransferases in cardiogenic shock
1961	West et al	Correlation of many cardiac factors and serum liver enzymes in heart failure
1961	Richman et al	Liver function test abnormalities in various forms of heart failure like acute, chronic, left sided etc.,
1962	Logan et al	Difference between serum enzyme elevation in heart failure and viral and drug induced hepatitis
1963	Refsum et al	Correlation between right sided heart failure and serum liver enzymes
1969	Whelan et al	Role of hypoxia in liver function test abnormalities
1973	Dunn et al	Liver function test abnormalities in congestive hepatopathy
1979	Bynum et al	Introduced the term “Ischaemic hepatitis”

YEAR	AUTHOR	OBSERVATION
1980	Nouel et al	Circulatory shock and fulminant hepatic failure
1981	Loosli et al	Alteration in liver serum enzymes, serum bilirubin, serum proteins and prothrombin time in ischaemic hepatitis
1985	Mace et al	Liver function derangements in congenital heart diseases
1997	Shovman et al	Hypotension and ischaemic hepatitis
2002	Rober et al	Clinical, hemodynaic, and histologic characteristics in cardiac hepatopathy
2005	Van Lingen et al	Jaundice as a presenting feature of heart failure
2006	Ebert et al	Massive elevation of liver serum enzymes in hypoxic liver injury.

CLINICAL COURSE AND MANAGEMENT

NATURAL COURSE OF HEART FAILURE



The outcome of patients with passive congestion of the liver relates to the underlying heart disease; rarely does liver disease cause significant morbidity or mortality in these patients.

If heart failure can be controlled medically, the early histologic changes may resolve. However prolonged, persistent hepatic congestion may result in cardiac cirrhosis. This is classically seen in patients with either constrictive pericarditis or prolonged mitral valve disease and secondary tricuspid insufficiency. Neverthless, cardiac cirrhosis does not in itself confer a poor prognosis[3] .

Ischaemic hepatitis is nearly always nonfatal and self-limited. The hepatic synthetic is usually impaired mildly, if at all; the prothrombin time is rarely prolonged by more than three seconds[3].

The overall prognosis is related to the severity of the underlying heart disease, not the severity of the liver disease[12]. Sherlock found no patients with cardiac cirrhosis showed stigmata of chronic liver disease or evidence of portosystemic shunting [8]. Esophageal varies have not been documented as a result of cardiac cirrhosis alone. Even after progression to cardiac cirrhosis, control of heart failure can lead to a regression of histologic and clinical liver abnormalities, with only latent cirrhosis left[3] .

The cornerstone in the management of congestive hepatopathy is treatment of the underlying heart disease. Jaundice and hepatic congestion may respond dramatically to therapy with diuretics. Maintenance of adequate cardiac output is the paramount importance. Liver dysfunction reverts to normal after successful treatment[3]. There is a dramatic fall in serum liver enzyme levels and serum bilirubin level after successful treatment of underlying heart failure. Solli et al, in 1992, and Squella et al, in 2003 found normalization of liver function tests in ischaemic hepatitis within five to ten days after the successful management of the underlying heart disease. Kumada et al, in 1989, observed liver function tests come to normal within a few days if congestive cardiac failure is adequately managed. The elevated liver serum enzymes activities decrease sharply with improvement in the patients' circulatory status [39].

MATERIALS AND METHODS

Setting

Medical wards, Institute of Internal Medicine, Government General Hospital, Chennai 600003.

Collaboration Department

The Department of Biochemistry, Government General Hospital, Chennai 600003 and Liver clinic Department, Government General Hospital, Chennai 600003.

Study Design

Single centre, cross-sectional and analytical study.

Period of Study

January 2006 to September 2006.

Consent

Informed consent was obtained in all cases.

Inclusion Criteria

Congestive heart failure in all age groups.

Heart failure definition

Heart failure is a clinical syndrome in which an abnormality of cardiac structure or function is responsible for the inability of the heart to eject or fill with blood at a rate commensurate with the requirements of the metabolizing tissues [53].

Mechanisms of heart failure [54]

1. Reduced ventricular contractility

    Eg. Myocardial infarction, cardiomyopathy.

2. Ventricular outflow obstruction

    Eg. Rheumatic aortic stenosis.

3. Ventricular inflow obstruction

    Eg. Rheumatic mitral stenosis.

4. Ventricular volume overload

    Eg. Rheumatic mitral regurgitation and aortic regurgitation.

5. Arrhythmia

    Eg. Atrial fibrillation.

6. Diastolic dysfunction

    Eg. Constrictive pericarditis.

Forms of heart failure [53,54]

1. Systolic heart failure

Eg. Dilated cardiomyopathy.

2. Diastolic heart failure

Eg. Hypertensive heart disease, constrictive pericarditis and HOCM.

3. Low output heart failure

Eg. Dilated cardiomyopathy, hypertensive heart disease, Rheumatic mitral and aortic stenotic valvular diseases etc..,

4. High output heart failure

Eg. Anaemia and Thyrotoxicosis.

5. Right sided heart failure

Eg. Cor pulmonale.

6. Left sided heart failure

Eg. Rheumatic mitral valvular diseases.

7. Biventricular heart failure

Eg. Coronary artery heart disease, dilated cardiomyopathy.

8. Acute heart failure

Eg. Heart failure which develops suddenly as in myocardial function, compensated heart failure aggravated by precipitating factors like respiratory infection, arrhythmia etc..,

9. Chronic heart failure

Eg. Heart failure develops or progresses slowly as in Valvular heart diseases and dilated cardiomyopathies.

Framingham criteria for diagnosis of congestive heart failure [53]

Major Criteria

1. Paroxymal nocturnal dyspnoea
2. Neck vein distension
3. Rales
4. Cardiomegaly
5. Acute pulmonary edema
6. S3 gallop
7. Increased venous pressure (> 16 cmH2O)
8. Positive hepatojugular reflex

Minor Criteria

1. Extremity edema

2. Night cough

3. Dyspnoea on exertion

4. Hepatomegaly

5. Pleural effusion

6. Vital capacity reduced by one-third from normal

7. Tachycardia (> 120 bpm)

Major Or Minor

Weight loss > 4.5 kg over 5 days' treatment

To establish a clinical diagnosis of congestive heart failure by these criteria, at least one major and two minor criteria are required.

Exclusion Criteria

1. History of alcoholism.

2. Past history of jaundice.

3. Recent intake of hepatotoxic and cholestatic drugs.

4. Presence of HBs Antigen and Anti HCV Antibodies.

5. Pregnancy.

6. Blood transfusion.

7. Hemolytic disorders.

8. Obstructive jaundice.

9. Infectious hepatitis.

Sample size

Sixty patients with various aetiologies of heart failure.

Selection of study materials

Among cases admitted with heart failure in the medical wards, government general hospital, sixty patients who had met the inclusion and exclusion criteria were taken up for study.

Selection of controls

Among patients who attended medicine outpatient department, government general hospital, for general health check-up, twenty persons were taken up as controls. Controls and study group were matched according to the age and gender. They are excluded from diseases which are thought to influence the study by approprite investigations.

Details of the study

After admission, complete history was elicited from all patients. After doing complete physical examination, clinical diagnosis of congestive heart failure and the possible aetiology of heart failure was made. Patients who were found to have haemodynamic imbalance were adequately stabilized with appropriate management.

After stabilization, they were subjected to complete investigations which included complete haemogram, plasma glucose, renal function tests, serum electrolytes, urine analysis, liver function tests, x-ray chest, ultrasonography of abdomen, electrocardiography and echocardiography etc..,

Thyroid function tests and pulmonary function patients were done in selected patients. After completing all investigations the results were assessed for the study.

All relevant investigations were done also in controls.

Liver size is assessed by ultrasonagram.

Liver function tests

A large number of tests have been proposed, but many provide similar information.

The liver carries out thousands of biochemical functions, most of which cannot be easily measured by blood tests. Laboratory tests measure only a limited number of these functions. No one test enables the clinician to accurately assess the liver's total functional capacity. To increase both the sensitivity and specificity of laboratory tests in the detection of liver disease, it is best to use them as a battery. Those tests usually employed in clinical practice are mentioned below.

1. Tests used as indices of uptake, conjugation, and excretion of anionic compounds

    - Serum total bilirubin (and direct and indirect).

2. Tests that reflect damage to hepatocytes

    - Serum aspartate and alaline aminotransferases.

3. Tests that reflect cholestasis

    - Serum alkaline phosphatase.

4. Tests that measure biosynthetic functions of the liver

    - Serum proteins
    - Serum albumin.
    - Prothrombin time

Serum bilirubin

Bilirubin, a breakdown product of the porphyrin ring of heme-containing proteins, is found in the blood in two fractions- a water soluble, conjugated, direct fraction and a lipid soluble, unconjugated, indirect fraction. In our laboratory specific agents are used to detect the quantity of bilirubin in the serum.

	Reagent	**Amount**	**Sample**	**Amount**
Total bilirubin	Total bilirubin Reagent & Sodium nitrite	1000 microliters 25 microlitres	Serum	50 microlitres
Direct bilirubin	Direct bilirubin Direct Reagent & Sodium nitrite	1000 microlitres 25 microlitres	Serum	50 microlitres

Indirect bilirubin = (Total bilirubin – Direct bilirubin)

METHOD : Erba semi autoanalyzer after ten minutes incubation.

Serum enzyme assays

The aminotransferases participate in gluconeogenesis by catalyzing the transfer of amino groups from aspartic acid or alanine to ketoglutaric acid to produce oxaloacetic acid and pyruvic acid, respectively. SGPT is a cytosolic enzyme, whereas SGOT is present as both cytosolic and mitochondrial enzymes. Elevation of the activity of these enzymes in serum is believed to be

the result of leakage from damaged cells and thus reflects hepatocyte injury. Hence, Serum liver aminotransferases are sensitive indicators of liver cell injury and most useful in recognising acute hepatocellular diseases. Alanine aminotransferase is found primarily in the liver whereas aspartate aminotransferase is found in many organ systems. The aminotransferases are normally present in the serum in low concentrations.

These enzymes are released into the blood in greater amounts when there is damage to the liver cell membrane resulting in increased permeability. However, there is a poor correlation between the degree of liver damage and the level of aminotransferases. Striking elevations occur with extensive hepatocellular injury as ischaemic hepatitis.

	Reagent	**Amount**	**Sample**	**Amount**
SGOT	OT reagent	500 microlitres	Serum	50 microlitres
SGPT	PT enzyme reagent & Starter reagent	400 microlitres 100 microlitres	Serum	50 microlitres

METHOD : Erba semi autoanalyzer.

The alkaline phosphatase is found in or near the bile canalicular membrane of hepatocytes. It is usually elevated in cholestasis. The normal serum alkaline phosphatase consists of many distinct isoenzymes found in various organs. Elevation of liver-derived alkaline phosphatase is not totally

specific for cholestasis and a less than threefold elevation can be seen in almost any type of liver disease. Isolated elevations of alkaline phosphatase can occur in congestive heart failure.

	Reagent	Amount	Sample	Amount
SAP	SAP reagent	500 microlitres	Serum	15 microlitres

METHOD : Erba semi autoanalyzer.

Serum proteins

The liver makes many circulating plasma proteins. Not surprisingly liver disease affects the plasma concentration of many of them. However the effects are complex and depend not only on changes in protein synthesis, but also on the effects of liver disease on the volume and distribution of extracellular fluids, on the half life of individuals proteins, on their catabolism by various tissues. There may also be changes in the metabolism of plasma proteins produced outside the liver. It is often normal when there are gross disturbances of individual components.

When the total level is either high or low its significance can only be interpreted by measurement of the major fractions. Measurement of total protein together with albumin is used to calculate globulin fraction by difference.

	Reagent	Amount	Sample	Amount
Serum Proteins	Serum protein reagent	1000 microlitres	Serum	10 microlitres

METHOD : Erba semi autoanalyzer.

Serum albumin

Albumin is the most abundant circulating protein. Liver is the only site of synthesis. When synthesis is reduced, the drop in plasma albumin is minimized by a reduction in its fractional catabolic rate. The serum albumin is widely regarded as a test of liver function, as if reflects hepatic protein synthesis. Low values can result from increased gastrointestinal or renal loss, increased catobolism, altered vascular permeability, or overhydration. Furthermore it may take many days before reduced synthesis causes an obvious change in serum albumin because it has a long half-life (about 20 days). Hence, serum albumin concentration should be interpreted with caution.

	Reagent	Amount	Sample	Amount
Serum albumin	Serum albumin reagent	1000 microlitres	Serum	10 microlitres

METHOD : Erba semi autoanalyzer.

Serum prothrombin time

With the exception of factor VIII, the blood clotting factors are made exclusively in hepatocytes. Their serum half-lives are much shorter than albumin, ranging from six hours for factor VII fo five days for fibrinogen. Serum prothrombin time collectively measures factors II, V, VII, and X. Biosynthesis of these factors depends on vitamin K.

	Reagent	**Amount**	**Sample**	**Amount**
PT	PT Reagent	200 microlitres	venous blood	100 microliters

PT reagent contains lyothilized human placental thromboplastin, $CaCl_2$ and preservatives.

METHOD : Autoanalyzer.

RESULTS

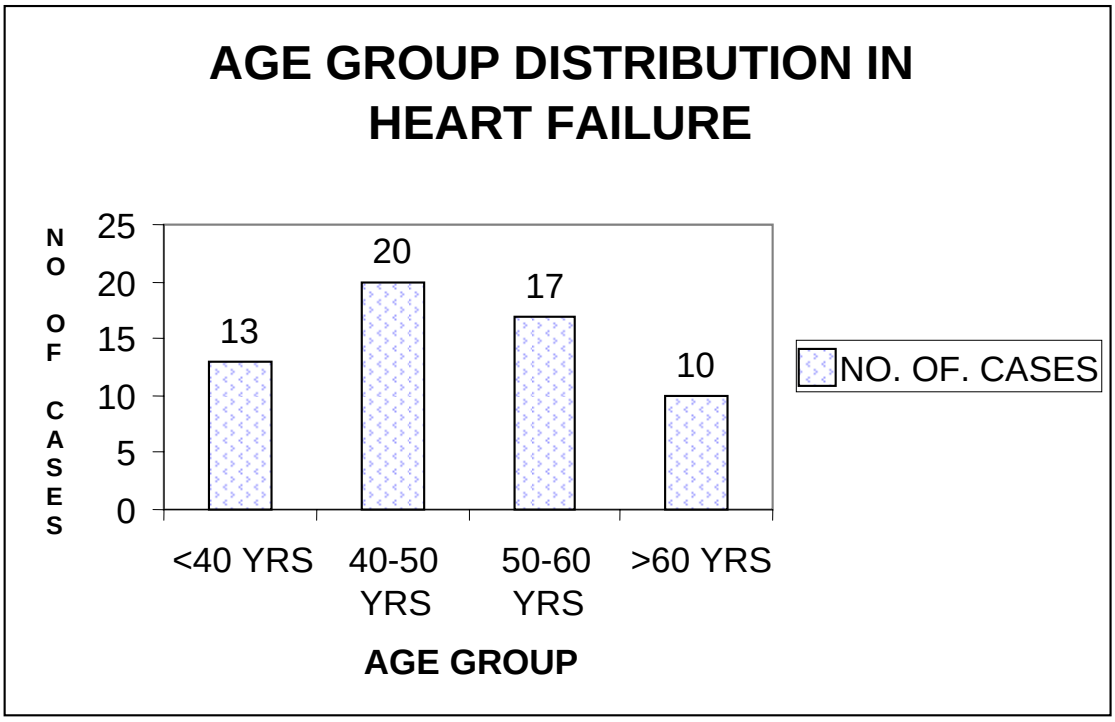
GENDER DISTRIBUTION IN HEART FAILURE

SEX	NO. OF CASES
MALE	36
FEMALE	24
TOTAL	60

MALE AND FEMALE RATIO = 1.5 : 1

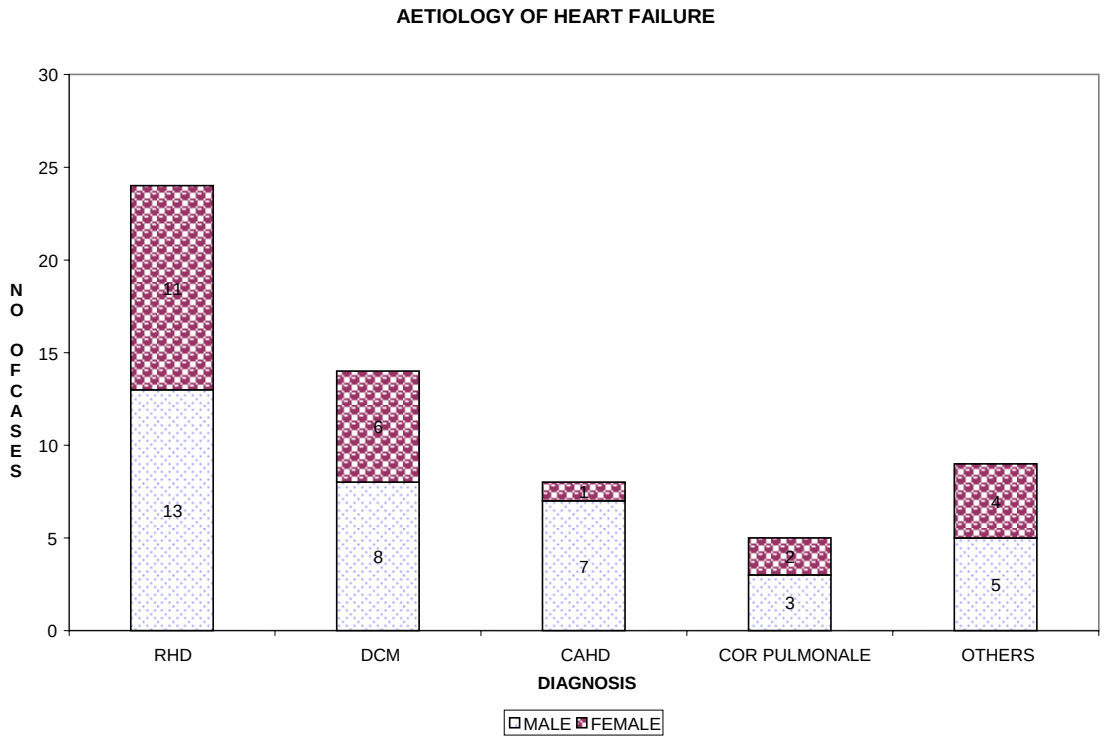
AGE GROUP DISTRIBUTION IN HEART FAILURE

AGE GROUP	NO. OF. CASES
<40 YRS	13
40-50 YRS	20
50-60 YRS	17
>60 YRS	10
TOTAL	60



AETIOLOGY OF HEART FAILURE

DIAGNOSIS	MALE	FEMALE	TOTAL	PERCENTAGE
RHD	13	11	24	40%
DCM	8	6	14	23.3%
CAHD	7	1	8	13.3%
COR PULMONALE	3	2	5	8.3%
OTHERS	5	4	9	15%
TOTAL	36	24	60	100%



DURATION OF HEART FAILURE

GENDER	DURATION	
	ACUTE	CHRONIC
MALE	2	34
FEMALE	3	21
TOTAL	5	55

PERCENTAGE OF JAUNDICE

GENDER	TOTAL NO. OF CASES	NO. OF CASES WITH JAUNDICE
MALE	36	7
FEMALE	24	5
TOTAL	60	12

PERCENTAGE OF JAUNDICE = 20%

PERCENTAGE OF HEPATOMEGALY

GENDER	TOTAL NO. OF CASES	NO. OF CASES WITH HEPATOMEGALY
MALE	36	22
FEMALE	24	16
TOTAL	60	38

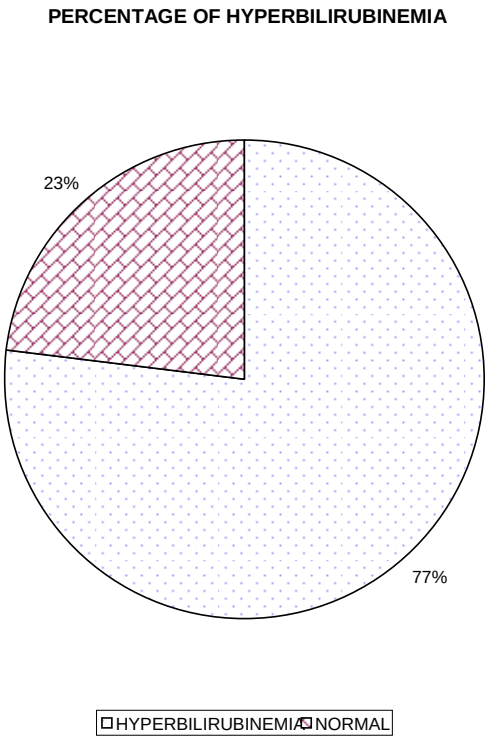
PERCENTAGE OF HEPATOMEGALY = 63%

PERCENTAGE OF HYPERBILIRUBINEMIA

GENDER	TOTAL NO. OF CASES	NO. OF CASES WITH HYPERBILIRUBINEMIA
MALE	36	26
FEMALE	24	20
TOTAL	60	46

PERCENTAGE OF HYPERBILIRUBINEMIA = 77%

PERCENTAGE OF HYPERBILIRUBINEMIA



PERCENTAGE OF ELEVATED SERUM AMINOTRANSFERASES

TOTAL NO. OF CASES	60
NO. OF CASES WITH ELEVATED AMINOTRANSFERASES	47

PERCENTAGE OF ELEVATED AMINOTRANSFERASES = 78%

PERCENTAGE OF ELEVATED SERUM ALKALINE PHOSPHATASE

TOTAL NO. OF CASES	60
NO. OF CASES WITH ELEVATED SERUM ALKALINE PHOSPHATASE	15

PERCENTAGE OF ELEVATED ALKALINE PHOSPHATASE = 25%

PERCENTAGE OF LOW SERUM PROTEINS

TOTAL NO. OF CASES	60
NO. OF CASES WITH LOW SERUM PROTEINS	43

PERCENTAGE OF LOW PROTEINS = 72%

PERCENTAGE OF LOW SERUM ALBUMIN

TOTAL NO. OF CASES	60
NO. OF CASES WITH LOW ALBUMIN	56

PERCENTAGE OF LOW ALBUMIN= 93%

PERCENTAGE OF PROLONGED PROTHROMBIN TIME

TOTAL NO. OF CASES	60
NO. OF CASES WITH PROLONGED PROTHROMBIN TIME	53

PERCENTAGE OF PROLONGED PROTHROMBIN TIME = 88%

S. NO.	VARIABLES	GROUP				P VALUE
		STUDY GROUP		CONTROL GROUP		
		MEAN	SD	MEAN	SD	
1.	EF (%)	51.10	7.83	61.44	4.00	<0.01**
2.	Liver Size (cm)	14.53	2.51	12.84	1.43	0.002**
3.	Total Serum Bilirubin (mg/dl)	1.81	1.16	0.88	0.08	<0.01**
4.	Conjugated Bilirubin (mg/dl)	0.18	1.17	0.05	0.06	<0.01**
5.	Unconjugated Bilirubin (mg/dl)	1.63	1.01	0.83	0.07	<0.01**
6.	SGOT (U/l)	113.55	77.68	42.44	21.67	<0.01**
7.	SGPT (U/l)	99.92	64.97	37.48	19.36	<0.01**
8.	SAP (U/l)	128.12	56.34	126.8	52.2	0.920
9.	Serum Protein (g/dl)	6.55	0.53	6.94	0.67	<0.005**
10.	Serum Albumin (g/dl)	3.27	0.56	4.04	0.35	<0.01**
11.	A/G Ratio	1.02	0.26	1.43	0.27	<0.01**
12.	Prothrombin time (sec.)	14.55	4.07	11.24	0.44	<0.01**

Note :

**P Value ≤ 0.01 = Significant at 1% level
*P Value 0.011 to 0.05 = Significant at 5% level
P Value >0.05 = Not Significant at 5% level

RANGE

S. NO.	VARIABLES	RANGE
1.	Liver Size	11 cm to 20 cm
2.	Total Serum Bilirubin	0.6 mg/dl to 5.2 mg/dl
3.	Serum Albumin	2.2 g/dl to 4.3 g/dl
4.	SGOT	16 U/l to 334 U/l
5.	SGPT	18 U/l to 360 U/l
6.	SAP	45 U/l to 310 U/l

CORRELATION COEFFICIENTS

	LIVER SIZE	TOTAL BILIRUBIN	CONJ. BILIRUBIN	UNCONJ. BILIRUBIN
Liver Size	-	r=0.57 p=<0.01	r=0.40 p=<0.02	r=0.58 p=<0.01
Total Bilirubin	r=0.57 p=<0.01	-	r=0.86 p=<0.01	r=1 p=<0.01
Conj. Bilirubin	r=0.40 p=<0.02	r=0.86 p=<0.02	-	r=0.81 p=<0.01
Unconj. Bilirubin	r=0.58 p=<0.01	r=1 p=<0.01	r=0.81 p=<0.01	-

Note :

'r' indicates correlation (eg. r value of 0.57 denotes 57% correlation)
'p' indicates significance (p value <0.01 indicates significance at 1% level)

t- test for

SGOT to SGPT RATIO

VARIABLE	NO. OF. CASES	MEAN	SD	P VALUE
STUDY GROUP	60	1.1974	0.476	0.984
CONTROL GROUP	25	1.1952	0.369	

Table values indicate SGOT to SGPT ratio is almost similar in both groups.

t-test for SGOT and SGPT

VARIABLE	r value	p value
SGOT	0.92	<0.01
SGPT		

Table values suggest a strong correlation between SGPT and SGOT which is considered to be significant at 1% level (p=<0.01)

SGOT VS UNCONJUGATED BILIRUBIN

		SGOT		P VALUE
		≤ 42	> 42	
Unconj. Bilirubin	≤ 0.83	50%	50%	0.003
	> 0.83	13%	87%	

Values indicate a significant correlation between SGOT and unconjugated bilirubin

S.NO.	VARIABLES	DURATION				P VALUE
		ACUTE		CHRONIC		
		MEAN	SD	MEAN	SD	
1.	Total Bilirubin	3.18	1.05	1.68	1.09	0.005
2.	SGOT	200.4	91.45	105.65	72.19	0.008
3.	SGPT	172.2	63.28	93.35	61.55	0.008
4.	Serum Albumin	3.46	0.42	3.25	0.57	0.433

Note :

p value <0.01 indicates significance at 1% level
p value > 0.05 indicates not significant at 5% level

S.NO.	VARIABLES	HYPOTENSION				P VALUE
		PRESENT		NORMAL BP		
		MEAN	SD	MEAN	SD	
1.	Total Bilirubin	3.93	1.14	1.69	1.06	0.001
2.	SGOT	239.33	54.12	106.93	73.21	0.003
3.	SGPT	173.33	4.16	96.05	64.37	0.044

Note:

p value <0.01 indicates significance at 1% level
p value 0.011 to 0.05 indicates significance at 5% level

DISCUSSION

To characterize the incidence and severity of liver function abnormalities in patients with heart failure, the present study analyzed liver biochemical profiles in sixty cases with heart failure of varied aetiologies and mechanisms. Innumerable references about the clinical and biochemical parameters about the hepatic circulation, hepatic function and the over all disturbance in the liver function secondary to heart failure of varied aetiologies have been correlated with the present study of sixty cases. Sincere effort has been made to correlate the results.

JAUNDICE

Clinical jaundice was present in 12 cases among total sixty cases. Present study showed 20% cases with jaundice in heart failure patients. We have found no correlation between the presence of jaundice and the duration of heart failure. Whereas heart failure patients with hypotensive episodes showed a strong correlation with clinical jaundice.

Jaundice was present in all three cases of heart failure with low blood pressure.

Dunn et al, in their study on the liver in congestive heart failure, observed 20% cases with jaundice[17]. White et al, observed jaundice in 21% of

their cases[25]. Van Lingen et al, observed only eight (1.2%) cases with jaundice in their retrospective study on jaundice as a presentation of heart failure in 661 cases. All eight patients had severe cardiac dysfunction. He found jaundice due to heart disease tends to be mild and the most common mechanism is hepatic passive congestion [47]. Richman et al, found jaundice in 5% cases[19].

Sherlock et al, in their study of 50 patients with heart failure, found eight cases with jaundice. She concluded jaundice in right heart failure results from congestion and greater the extent of zone 3 necrosis the deeper the jaundice[8].

AUTHOR	PERCENTAGE OF JAUNDICE
Dunn et al	20%
White et al	21%
Van Lingen et al	1.2%
Richman et al	5%
Sherlock et al	16%
Present study	20%

HEPATOMEGALY

Liver size more than 13 cm by ultrasonography is defined as hepatomegaly in our study. Enlarged liver is seen in 63% of cases which is considered to be highly significant (P = 0.002) in heart failure patients.

Maximum size of the liver goes up to 20 cm which is seen in three patients. Present study revealed a significant (P = < 0.01) correlation between increase in liver size and increase in both total (r = 0.57) and unconjugated (r = 0.58) serum bilirubin levels. Whereas there is no significant correlation between hepatomegaly and conjugated serum bilirubin levels. Dunn et al, found 95% of hepatomegaly in congestive heart failure patients[17]. White et al, observed 95 to 99% cases with hepatomegaly. Jurg Reichen et al, observed hepatomegaly in 95 to 99% of patients in right sided heart failure [20].

AUTHOR	PERCENTAGE OF HEPATOMEGALY
Dunn et al	95%
White et al	95-99%
Jurg Reichen et al	95-99%
Present study	63%

HYPERBILIRUBINEMIA

Total serum bilirubin level more than 0.9 mg/dl is taken as hyperbilirubinemia according to our study. Serum hyperbilirubinemia is seen in 77% of heart failure patients in the present study which is considered as highly significant (P = < 0.01) in comparison with control cases. The maximum level goes up to 5.2 mg/dl, which is seen in two patients.

The present study revealed a significant (P = < 0.01) correlation (r = 1) between the total and the unconjugated fraction. Unconjugated fraction values were found to be higher than the conjugated fraction. Dunn et al, observed mild elevation of the serum bilirubin in 70% of congestive heart failure patients. He found the total serum bilirubin is usually less than 3 mg/dl, with a high unconjugated fraction[17]. Kubo et al, found hyperbilirubinemia within the value of 2.5 mg/dl[20]. Sherlock found the serum bilirubin level usually exceeds 1 mg/dl and in about one-third it is more than 2 mg/dl[8].

AUTHOR	PERCENTAGE OF HYPERBILIRUBINEMIA
Sherlock et al	68%
Felder et al	52%
Evans et al	26%
White et al	40%
Dunn et al	70%
Present study	77%

Present study shows total serum bilirubin level is higher in acute heart failure than in chronic heart failure. There is significant (P = 0.005) correlation between elevated total serum bilirubin and acute heart failure when compared to chronic heart failure.

Richman et al, described liver function abnormalities in 175 patients with congestive heart failure. They found acute heart failure is associated with more elevation of total serum bilirubin[19].

Present study found an unusually high total serum bilirubin level in patients presented with hypotension. A significant (P = 0.001) correlation was found in those cases. Bilirubin levels are higher even than in acute heart failure. Shovman et al, described ischaemic hepatitis in congestive heart failure after an episode of hypotenion.

They found a rise in serum bilirubin in their study. They finally concluded ischaemic hepatitis should be considered whenever acute hepatitis follows a recent episode of hypotension [40].

Virtually any cause of shock or hemodynamic instability can result in ischaemic injury to the liver[3]. The main mechanism proposed for the development of centrilobular necrosis is a severe decrease in cardiac output, the resulting hepatic hypoxia causing damage to the hepatocytes[9]. The serum total bilirubin level rises above four times the upper limit of normal in ischaemic hepatitis[3].

Present study revealed more than threefold rise in serum bilirubin level in patients with hypotension. Gibson et al, observed abnormal liver function tests due to ischaemic hepatitis secondary to acute illness associated with a fall

in cardiac output and systemic hypotension, characterized by marked increase in serum bilirubin[12].

SERUM AMINOTRANSFERASES

SGOT level of more than 42 U/l and SGPT level of more than 37 U/l are taken as elevated levels according to our study. Present study revealed 78% cases with elevated liver serum aminotransferasesin sixty heart failure patients which is considered as highly significant (P = < 0.01).

Maximum serum level goes up to 360 U/l in SGOT and up to 334 in SGPT. Present study reveals a significant (P = < 0.01) correlation between elevation of SGOT and SGPT in heart failure patients. Again a significant (P = 0.003) correlation was identified between elevation of SGOT and elevation of unconjugated bilirubin levels. Preseny study found SGOT levels are higher than SGPT levels.

Richman et al, found though both aminotransferases were high in his study on alterations in liver function in congestive heart failure with particular reference to serum enzymes, SGPT levels were less marked than, those of SGOT levels.

The serum AT levels are only mildly elevated in congestive heart failure, usually to two to three times normal levels[3]. Kubo et al, found

significantly higher levels of AT levels in severe heart failure patients[20]. Nanji et al, observed high SGOT values in congestive heart failure patients. They observed congestive heart failure usually features a mild to moderate increase in SGOT level. A marked increase in SGOT level may occur rarely[43].

In the present study, ratio between SGOT and SGPT was found to be not significant in comparison with control cases (P = 0.984). Whereas there is a significant (P = < 0.01) correlation (r = 0.92) between elevation of SGOT and SGPT levels in the study group.

Duration of heart failure affects serum levels of aminotransferases. Present study observed serum aminotransferases' levels are higher in acute heart failure than in chronic heart failure which is highly significant (P=0.008). Study reveals threefold to eightfold rise in aminotransferases' level in acute heart failure. Heart failure patients with hypotension were found to have a massive elevation of aminotransferases levels.

In a series of 175 patients with acute and chronic heart failure, Richman et al, observed higher SGOT levels in acute heart failure than chronic heart failure[19].

Sherlock et al, found very high values of SGOT can occur with an acute onset of severe heart failure, especially if it is associated with hypotension or

shock[8]. However, high serum aminotransferaes levels have been described in the setting of heart failure with minimal or no hemodynamic instability[9].

Increased venous congestion and decreased hepatic perfusion both contribute to the elevation of aminotransferases, although centrilobular hypoxia and/or necrosis are probably the major factors[48]. Henrion et al, studied 142 cases of hypoxic hepatitis. He found in congestive heart failure and acute heart failure, the hypoxia of the liver resulted from decreased hepatic blood flow (ischaemia) due to left sided heart failure and from venous congestion secondary to right sided heart failure. In chronic respiratory failure, liver hypoxia was mainly due to profound hypoxemia. A shock state was observed in only about 50% of cases[51].

Present study revealed the ratio of SGOT to SGPT is 1.2 (mean) in both study and control groups which is considered to be not significant (P = 0.984). It excludes the presence of alcoholic hepatitis since this ratio is characteristically greater than two in such cases[49].

SERUM ALKALINE PHOSPHATASE

Serum alkaline phosphatase level more than 127 U/l is taken as higher than normal according to our study. Present study observed elevation of serum alkaline phosphatase in 15 cases (25%) among 60 heart failure cases which is considered to be not significant (P = 0.920). Maximum level goes up to 310 U/l

which is seen in one patient. In most of the cases the level is less than twofold rise.

Kubo et al and Sherlock et al, found rise in serum alkaline phosphatase by about 10 to 20% cases with congestive heart failure [8,20]. Richman et al, found intrahepatic biliary obstruction due to a high intrahepatic pressure may play a role in the alkaline phosphatase rise with congestive heart failure[19].

SERUM PROTEINS AND SERUM ALBUMIN

The estimation of total plasma protein alone is of relatively little value. It is often normal even when there are gross differences of individual components. When the total level is either high or low its significance can only be interpreted by measurement of the major fractions [48].

Present study has taken serum level less than 6.9 g/dl as evidence for decreased serum proteins level and serum level less than 4.0 g/dl as evidence for hypoalbuminemia. Low serum proteins level was found in 72% of cases and low albumin values were found in 93% of cases with sixty heart failure patients which are considered to be highly significant ($P = < 0.01$). The ratio of serum albumin to globulin below 1.43 is considered evidence for low A/G ratio according to the present study. Present study observed low A/G ratio in 93% of cases which is highly significant ($P = < 0.01$). Felder et al, found decresed serum albumin level in 26% of cases[24]. Naresh et al, found low serum albumin

level in 39% of cases with congestive heart failure. Richman et al, found low serum albumin in 30 to 50% of patients with congestive heart failure. He observed the incidence, and degree of change appears to be similar in acute and chronic heart failure[19]. Present study also revealed there is no significance (P = 0.433) in serum albumin level with acute heart failure when compared to chronic heart failure.

The serum albumin level does not correlate with the degree of histological damage to the liver[19,24]. Present study revealed extremely low serum albumin in most of the patients. Changes in serum albumin concentration should be interpreted with caution because many conditions other than liver disease are associated with low albumin levels.

This low albumin value could be attributed to many factors which includes increased gastrointestinal or renal loss, reduced dietary intake of protein as a result of decreased appetite, increased catabolism, leakage from a congested intestine and overhydration.

Thus a low serum albumin level is not specific for liver disease.

SERUM PROTHROMBIN TIME

Serum prothrombin time is often prolonged in congestive heart failure[17,19,25]. Present study found prolonged prothrombin time in 88% of

cases with sixty heart failure patients which is considered highly significant (P = < 0.01). PT more than 11 seconds is taken as abnormal value according to the study. White et al, found prolonged PT in 80 to 90% of cases with acute and chronic heart failure[25]. Present study observed there is only a mild elevation in prothrombin time. Caution should therefore be exercised when treating patients in heart failure with oral anticoagulants.

SUMMARY

Abnormal liver enzymes and liver function in congestive cardiac failure has long been recognized and occurs quite frequently in acute and chronic failure[19]. The present study was undertaken to identify alterations in the liver biochemical profiles in relation to congestive heart failure and also to show their significance with respect to the duration of heart failure.

Sixty cases with heart failure of various aetiologies and twenty healthy controls were included in the study. In the present study, number of male cases were higher than number of female cases. Among sixty total cases 36 male and 24 female cases were present. Higher number of cases were found within the age group of 40 to 50 years followed by the age group of 50 to 60 years.

The present study revealed rheumatic heart disease is still the leading cause of heart failure in our set up. Among the total heart failure cases, 40% were due to rheumatic heart disease. Dilated cardiomyopathies represent about 23% of cases. Heart failure secondary to coronary artery heart disease is seen in about 13% of cases. We have found five cases with acute heart failure and three cases with hypotension.

Present study revealed a strong correlation between liver function derangements and the above cases.

Serum bilirubin, serum aminotransferases, serum alkaline phosphatase, serum proteins, serum albumin and prothrombin time were the liver biochemical tests used in the study. Echocardiography and ultrasonography of the liver were also done in all cases.

Present study has found a strong relationship between liver function derangements and heart failure cases. The study observed 20% of cases with jaundice. Among sixty cases liver enlargement was seen in 63% of cases. Increased liver size is strongly correlated with hyperbilirubinemia. Though the conjugated fraction of bilirubin is also elevated, the levels of unconjugated fraction were higher.

Serum aminotransferases were elevated in 78% of cases unlike serum alkaline phosphatase which is increased only in 25% of cases. There found to be a significant correlation between rise in unconjugated bilirubin and elevation of serum aminotransferases. Study revealed marked alterations in liver function with acute heart failure and during hypotension when compared to chronic heart failure.

Low serum proteins and serum albumin levels are seen in many of the cases. Various factors play in causing these changes which have already been discussed. Serum prothrombin time, though prolonged in 88% of cases, the changes were only mild.

CONCLUSION

The present study undertaken shows a significant changes in liver biochemical profiles in patients with congestive heart failure. These changes are found to be useful in assessing the duration and severity of heart failure.

The liver performs a diverse array of biochemical, synthetic, and excretory functions, and as a result, no single biochemical test is capable of providing an accurate global assessment of hepatic function. Hence, clinical evaluation, a complete biochemical profile, the underlying cause and radiologic imaging are necessary to interpret the liver function tests.

The altered liver functions in heart failure patients are often reversible. The present study suggests an early detection of liver function abnormalities in heart failure patients. Treatment should mainly be focused on the underlying heart disease. Regression in liver derangements occurs after successful treatment of heart failure in most of the cases.

Present study could not follow up all sixty cases to assess the regression of liver function abnormalities due to practical concerns.

Maintenance of stable hemodynamic status is of paramount importance. Even in ischaemic hepatitis, the liver is able to regenerate and recover normal function if appropriate treatment is applied to the underlying heart disease.

Care must be taken to avoid excessive diuresis in patients with severly impaired cardiac output, which can impair hepatic perfusion and precipitate zone 3 necrosis. Since many of our patients showed prolonged serum prothrombin time, cautious use of oral anticoagulants is advised in those cases.

So, present study concluded early identification of changes in liver biochemical profiles is not only useful in assessing the duration and severity of heart failure but also in preventing permanent hepatic damage.

BIBLIOGRAPHY

1. Lautt WW, Greenway CV, Conceptual review of the hepatic vascular bed. Hepatology 1987; 7: 952-963.

2. Rappaport, A.M. (1958). The structural and functional unit in the human liver, Anat. Rec., 130, 673-90

3. Eugene R Schiff, Michael F Sorrell, Willis C Maddrey (edrs), Schiff's Diseases of the liver, ninth edition, Volume 2, 2003, Section 49, 1327-1336

4. Greenway, Physil Rev, 51 : 23

5. Acero, Gastro Hepato, 1984; 7:334, Hepatic blood flow in heart failure.

6. Rapaport E, Weisbart MH, and Levine M. The splanchnic blood volume in congestive heart failure. Circulation, 1958; 18: 581-7.

7. Safran AP, Schaffner F, Chronic passive congestion of the liver in man: electron microscopic study of cell atrophy and intralobular fibrosis, American Journal Of Pathol 1967; 50 : 447-463.

8. Sherlock S. The liver in heart failure : relation of anatomical, functional and circulatory changes British Heart Journal, 1951; 13 : 273-293.

9. Cohen JA, Kaplan MM, Left Sided heart failure presenting as hepatitis. Gastroenterology 1978; 74: 583 – 587.

10. Seeto RK, Fenn B, Rockey DC. Ischaemic hepatitis: Clinical presentation and pathogenesis. American Journal Of Medicine 2000; 109: 109-113.

11. Henrion J, Minette P, Colin L, et al, Hypoxic hepatitis, Journal Of Hepatology 1999; 29 : 427-433.

12. Gibson PR, Dudley FJ. Ischaemic Hepatitis : Aust NZ Journal Of Medicine 1984; 14: 822 – 825.

13. Gitlin N, Serio KM Ischemic Hepatitis: widening horizons. American Journal Of Gastroenterology 1992; 87: 831 – 836.

14. Shibayama Y. The role of hepatic venous congestion and endotoxaemia in the production of fulminant hepatic hepatic failure secondary to congestive heart failure. Journal Of Pathology. 1987; 151; 13: 273.

15. Moussavian SN, Dincsoy HP, Goodman S, et al. severe hyperbilirubinemia and coma in chronic congestive heart failure. Digestive Disease Sciences, 1982; 27: 175-180.

16. Logan RG, Mowry FM, Judge RD. Cardiac failure simulating viral hepatitis. Ann Intern Med 1962; 52: 784 -788.

17. Dunn GD, Hayes P, Breen KJ et al. The liver in congestive heart failure: a review. American Journal Of Medical Sciences 1973; 265: 174 -189.

18. West et al, American Journal Of Medical Sciences, 1961; 241: 3501.

19. Richman SM, Delman AJ, and Grab D. Alterations in indices of liver function in congestive heart failure with particular reference to serum enzymes. America Journal of Medicine, 1961; 30: 211 – 25.

20. Kubo SH, Walter BA, John DHA, Clark M and Cody RJ, Liver function abnormalities in chronic hear failure : influence of systemic hemodynamics. Archives of Internal Medicine, 1987; 147: 1227-9.

21. Nouel O, Henrion J, Bernuau J et al. Fulminant hepatic failure due to transient circulatory failure in patients with chronic heart diseases Digestive Disease Sciences, 1980; 25: 49 – 52.

22. Bynum TE, Boitnott JK, Maddrey WC. Ischaemic hepatitis. Digestive Disease Sciences 1979; 24: 129 – 135.

23. Tidsskr Nor LargeForen, Serum aminotransferases and treatment of heart failure. 1992 may 30; 112(14): 1827-8.

24. Johannea Bircher, Gean-Pierre Benhanou, Neil McIntyre, Juan Rodes (edrs),Oxford Textbook Of Clinical Hepatology, second edition, Volume 2, 1999, 503-513,1671-1675,

25. White TJ, Leevy CM, Brusia AM, and Gnassi AM. The liver in congestive heart failure. American Heart Journal, 1955; 49 : 250-7.

26. Robbins and Cotran, Pathologic Basis of Diseases, 7th edition, 2004, 918.

27. Lefkowith and Mendez (1986). Journal of Hepatology 147; 1227-1230 Histology in Congestive heart failure and shock

28. Garvin CF, Cardiac cirrhosis, American Journal Of Medical Sciences, 1943; 205: 515-518.

29. Killip T, Payne MA. High serum transaminage activity in heart disease : Circulatory failure and hepatic necrosis. Circulation 1960; 21: 646-660.

30. Yoshiko Samshima, Serum enzymes in congestive heart failure, circulation 28;92, 1964.

31. Evans American Journal Of Medicine, 1952; 13: 704 Altered liver functions in congestive heart failure.

32. Shorey j, Schenker S, Combes B. Effect of acute hypoxia on hepatic excretory function. American Journal Of Physiology 1969; 216: 1441-1452.

33. Whelan G, Pierce, Schenker S, et al. Hepatic function in patients with hypoxaemia due to chronic pulmonary disease. Aust Ann Medicine 1969; 18: 243-247

34. Kisloff B, Schaffer G. Fulminant hepatic failure secondary to congestive cardiac failure, American Journal Of Digestive Diseases 21(10): 895-900, 1976

35. Kaymakcalan, congestive heart failure as a cause of fulminant hepatic failure, American Journal of medicine 65 (2) : 384; August 1978.

36. Shouvman O, George J, Shoen Feld Y, 1997 April, Hare Fuah, 132 (7) : 459-60, 527. Ischaemic hepatitis in congestive heart failure after an episode of hypotension.

37. Arcidi JM, Moore GW, and Hutchins GM. Hepatic morphology in cardiac dysfunction : a clinicopathologic study of 100 subject at autopsy. American Journal of Pathology, 1981;104 : 160-5.

38. Ross RM. Hepatic dysfunction secondary to heart failure. American Journal of gastroenterology 76 (6): 511-8, 1981 Dec

39. Nanji AA, clin Biochem. 1983 April ; 16(2) 76-8 markedly increased serum aspartate aminotransferase activity in congestive cardiac failure

40. Mace, American J Dischild, 1985; 139 : 60 Congenital heart disease and its association with liver disease.

41. Arora, American Journal of Gastroenterology, 1993, 88; 430.

42. Robert P Myers et al, cardiac hepatopathy : Clinical, hemodynamic and histologic characteristics and correlations. Volume 37, Issue 2, Hepatology Pages 393 – 400, 10 – 1053 / j hepo. 2003.50062.

43. Van Lingen R, Jaundice as a presentation of heart failure, JR Soc Med 2005 August ; 98 (8) : 357 – 9.

44. Mark Feldman, Lawrence S Friedman, Marvin Sleisinger (edrs), Gastrointestinal and Liver Disease, pathophysiology/ Diagnosis/ Management 7 th edition, Volume 2, 2002. 1227-1231

45. Sheila Sherlock, James Dooley (edrs), Diseases of the liver and biliary system, 11 th edition, 2002, 199-203.

46. Henrion Jean; Schapira, Michael; Luwaert, Raymond: Colin, Lucien; Delannoy, Andre; Heller, Francis R. Medicine. 82(6): 392-406,2003. hypoxic hepatitis: Clinical and Hemodynamic study.

47. Naresh Bhu. Changes in liver function in congestive cardiac failure, current medical practice 4:144,1960.

48. Eugene Braunwald, Anthony S. Fauci, Dennis L. Kasper, Stephen L. Hauser, Dan L. Longo, Larry jameson (edrs), Harrison's principles of internal medicine, 16 th edition, volume 2, 2005, 1367-1371.

49. Christopher Haslett, Edwin R. Chilvers, Nicholas A. Boon, Nicki R. Colledge, John A. A. Hunter. Davidson's principles and practice of medicine, 19 th edition, 2002, 381-384.

ABBREVIATIONS

AT - Aminotransferase

HBs Ag - Hepatitis B surface antigen

Anti HCV Abs -Anti hepatitis C virus antibodies

SGOT - Serum glutamic oxaloacetic transaminase

SGPT – Serum glutamic pyruvic transaminase

PT – Prothrombin time

SAP – Serum alkaline phosphatase

$CaCl_2$ - Calcium chloride

A/G ratio – Albumin globulin ratio

PROFORMA

Name

Age

Sex

MRD No.

PRESENTING COMPLAINTS	**DURATION**
Chest pain	
Breathlessness	
Palpitations	
Syncope	
Cough	
Haemoptysis	
Swelling of legs	
Oliguria	
Fever	
Other symptoms	

PAST HISTORY	**DURATION**
Similar illness in the past	
Diabetes mellitus	
Hypertension	
Coronary artery heart disease	
Bronchial asthma	
Jaundice	

Rheumatic fever

Pulmonary tuberculosis

Transient ischaemic attacks

Abortion / Exposure to sexually transmitted diseases

PERSONAL HISTORY

Smoking

Alcoholism

FAMILY HISTORY

Hypertension

Diabetes mellitus

Coronary artery heart disease

CLINICAL EXAMINATION

Consciousness

Orientation

Temperature

Anaemia

Jaundice

Cyanosis

Clubbing

Pedal edema

Lymph node enlargement

Jugular venous pressure

Signs of infective endocarditis

Signs of liver failure

Pulse

Blood pressure

Respiratory rate

CARDIOVASCULAR SYSTEM

Parasternal heave

Abnormal pulsations

Heart sounds and murmurs

RESPIRATORY SYSTEM

Respiratory rate

Breath sounds

Added sounds

ABDOMEN

Appearance

Ascites

Hepatomegaly

Spleenomegaly

CENTRAL NERVOUS SYSTEM

Higher functions

Cranial nerves

Spinomotor system

Sensory system

Cerebellar system

Spine and cranium

DIAGNOSIS

INVESTIGATIONS

Blood hemogram

Urine routine

Blood sugar

Blood urea and serum creatinine

Serum electrolytes

HBs Ag

Anti HCV Abs

Electrocardiography

Echocardiography

Chest x ray

Liver function tests -	Serum bilirubin	Total
		Direct
		Indirect
	SGOT	
	SGPT	
	SAP	
	Serum proteins	
	Serum albumin	
	A/G ratio	

Prothrombin time

Ultrasonography of abdomen